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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,808	02/19/2002	Manas Kumar Majumdar	08702.0086-00000	7146

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EXAMINER
ANDRES, JANET L

ART UNIT PAPER NUMBER

1646

DATE MAILED: 09/26/2003

14/

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/078,808

Applicant(s)

MAJUMDAR ET AL.

Examiner

Janet L. Andres

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 11,12 and 21-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 11,12 and 21-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 19 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in Paper No. 13 is acknowledged. Claims 11, 12, and 21-31 are pending and under examination in this office action.

Specification

2. The use of the trademarks HELISTAT on p. 19, line 27, FICOLL-PAQUE on p. 22, line 5, and PHOTOSHOP on p. 32, line 10, has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 11 and 12 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by U.S. patent 6,150,328 (Wang et al., 2000).

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The '328 patent teaches the administration of BMP-2 to treat bone and cartilage defects. See example III, columns 9 and 10, and claims 1-7, which are drawn to a method of cell therapy that would result in the administration of the protein. Administration of BMP-2 would inherently result in effects on IL-1, regardless of whether the effects were recognized at the time. Thus the '328 patent anticipates methods of affecting IL-1 by administering BMP-2.

5. Claims 11 and 12 are also rejected under 35 U.S.C. 102(e) as being anticipated by U.S. patent 6,287,816 B1 (Rosen et al., filed 1994).

The '816 patent teaches administration of BMP-9 to treat bone, cartilage, and liver defects. See column 5, lines 13-67, column 20, lines 25-26, and claims 23-27. Administration of BMP-9 would inherently result in effects on IL-1, regardless of whether the effects were recognized at the time. Thus the '816 patent anticipates methods of affecting IL-1 by administering BMP-9.

6. Claims 21-31 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 00/29552 (Kavalkovich et al., 2000).

WO 00/29552 teaches an alginate layer system formed by seeding mesenchymal stem cells (MSCs) in alginate. These MSCs are known in the art to express CD105 (endoglin); see Barry et al., *Biochem. Biophys. Res. Comm.* 1999, vol. 265(1), pp. 134-139. WO 00/29522 teaches that alginate constructs can be formed using non-cultured populations of MSCs (p. 10, lines 10-19) and that the constructs can be used for cartilage regeneration (p. 5, lines 26-29). WO 00/29522 further teaches that BMP-2 can be included as a chondrogenic agent (p. 8, lines 21-24). WO 00/29552 thus anticipates method of administering compositions comprising non-

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expanded CD 105+ cells to regenerate cartilage, and additionally anticipates methods of administering such cells in combination with a matrix and/or with a BMP.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 21-31 are also rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/29552 in view of the '816 patent. WO 00/29552 teaches as set forth above but fails to teach co-administration of BMP-9. The '816 patent teaches that BMP-9 can be used to treat cartilage defects; see paragraph 5 above. It would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of WO 00/29552 with the '816 patent to co-administer BMP-9 with MSCs. One of ordinary skill in the art would have been motivated to do so because the two treatments are drawn to the same purpose. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

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“It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art.”

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 21-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of promoting chondrogenesis using MSCs in an alginate matrix, does not reasonably provide enablement for all methods of promoting chondrogenesis using MSCs, as claimed in claims 21-29, for methods using all bone marrow cells, as claimed in claims 21 and 26-28, or generally for repairing “tissue” as claimed in claims 28-31. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman*, (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands*, 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The instant specification and the prior art teach that non-tissue culture expanded MSCs in an alginate matrix can undergo chondrogenic differentiation, and that they can be implanted into

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defects. However, neither the prior art nor the specification teach chondrogenesis of non-tissue culture expanded cells as broadly claimed. Chondrogenic differentiation of MSCs is a complex process that generally requires a matrix or other three-dimensional structure; see, for example, WO 96/28359 and WO 98/32333, each of which teaches the use of a matrix or three-dimensional structure, as well as WO 00/29552, cited above; even using such approaches, success *in vivo* has been limited. The specification provides no guidance to indicate that non-expanded cell populations or any other cells could be used without such a structure; given the teachings of the prior art and the lack of direction provided, one of skill would not predict that such approaches would be successful.

Claims 21 and 26-28 encompass all bone marrow cells. However, what is known in the art is that CD 105+ cells are pluripotent. See, for example, Barry et al., cited above. These cells comprise only a small fraction of bone marrow cells; see WO 98/32333, p. 1. Thus one of skill in the art could not predictably use bone marrow cells as broadly claimed to promote chondrogenesis; only the small population of CD 105+ cells are known to have this ability.

Claims 28-31 encompasses repair of all tissue; since what is taught, exemplified, and claimed, is chondrogenesis. Thus one of skill in the art would expect to be able to repair cartilage, but not all "tissue", which would presumably include all cell types found in the body.

Thus, since the claims are broadly drawn, and neither the specification nor the prior art provides guidance commensurate in scope with what is claimed, it would require undue experimentation for one of skill in the art to practice the invention as broadly claimed.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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12. Claims 11 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are drawn to methods of “blocking or suppressing the inhibitory effect of IL-1”. IL-1 has many effects and one of skill in the art would not know what it was that Applicant intended to block.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 872-9306 or (703) 872-9307 for after final communications.

Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].


All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly

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set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.
September 25, 2003


JANET ANDRES
PATENT EXAMINER